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Volumetric versus single slice measurements of core abdominal muscle for sarcopenia.

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Measurements of core abdominal muscle for sarcopenia.

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NOTE: qualifications are reported as highest clinical followed by highest academic qualification.

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ABSTRACT

Objectives

We investigated whether total psoas muscle area (TPMA) was representative of the total psoas muscle volume (TPMV). Secondly, we assessed whether there was a relationship between the two commonly used single slice measurements of sarcopenia, TPMA and total abdominal muscle area (TAMA).

Methods

Pre-operative CT imaging of 110 patients undergoing elective endovascular aneurysm repair were analysed by two trained independent observers. TPMA was measured at individual vertebral levels between the second lumbar vertebrae and sacrum. TPMV was also estimated between the second lumbar vertebrae and sacrum. TAMA was measured at the third lumbar vertebrae (L3). Observer differences were assessed using Bland-Altman plots. Associations between the different measures were assessed using linear regression and Pearson's correlation.

Results

We found single slice measurements of the TPMA to be representative of the TPMV at individual levels between L2 to the sacrum. The strongest association was seen at L3 (adjusted regression coefficient 16.7, 95% CI 12.1 to 21.4, $p<0.001$). There was no association between TPMA and TAMA (adjusted regression coefficient -0.7, 95%CI -4.1 to 2.8, $p=0.710$).

Conclusions

We demonstrate that measurements of the TPMA between L2 to the sacrum are representative of the TPMV, with the greatest association at the third lumbar vertebrae. There was no association between the TPMA and TAMA.

Advances in knowledge

We demonstrate that a single slice measurement of TPMA at L3 is representative of the muscle volume, contrary to previous criticism. Future sarcopenia studies can continue to measure TPMA which is representative of the TPMV.

MAIN TEXT

Introduction

Sarcopenia is a condition that is categorised by low skeletal muscle mass and declining function. It is associated with worse patient outcomes and is an increasing problem due to a rapidly ageing population (1, 2). The European Working Group on Sarcopenia in Older People have recognised this and have recommended the routine assessment for sarcopenia in all patients aged above 65 years (2). Therefore, the quantification of core abdominal muscles as a surrogate marker for sarcopenia has become an increasingly popular in clinical research. The total psoas muscle area (TPMA) or the total abdominal muscle area (TAMA) from single slice computed tomography (CT) imaging at the endplates of the third or fourth lumbar vertebrae are the two commonest methods of quantifying sarcopenia (1). However, at present the optimum vertebral level to measure the TPMA is yet to be validated.

As muscles are complex three-dimensional structures, the use of single slice two-dimensional measurements of these may be criticised as being a poor representation to assess sarcopenia. The association between single slice TAMA and volumetric measurements of total abdominal muscle on CT imaging has been previously described and validated (3-5). Furthermore gender-specific cut-off values for TAMA have also been proposed which have been demonstrated to correlate with mortality (6). The assessment of the patients muscle volume using an automated quantification method with specialist software has been shown to be a better prognostic marker than area alone (7). However similar correlations are yet to be validated between single slice measurement of TPMA and three dimensional volumetric assessment of the psoas muscle (6).

The heterogeneity of the different methods of quantifying sarcopenia, TPMA and TAMA, currently make it difficult to compare and derive cut-of values for sarcopenia from single slice imaging. Measuring TAMA is more time consuming and often requires the use of specialist software. However, we have previously demonstrated that the TPMA can be easily and consistently measured on any picture archiving communications system (PACS) viewer (8). The identification of an interchangeable relationship between TPMA and TAMA may facilitate comparative analysis of previously reported outcomes and derive clinically uniform cut-off values defining sarcopenia applicable to the general patient population (1).

In this study, we investigated whether there was a relationship between total psoas muscle volume (TPMV) and TPMA, and identify the vertebral level at which the TPMA is most representative of the muscle volume. Secondly, we investigated the relationship between single slice measurements at the third lumbar vertebrae of TPMA and TAMA.

Methods

We analysed prospectively collected data from patients who have had an elective endovascular aneurysm repair (EVAR) for an abdominal aortic aneurysm (AAA).

Study population

We randomly selected pre-operative abdominal CT angiogram (CTA) scans routinely performed as part of the assessment for intervention. All scans were performed in the supine position with a breath-hold to minimise motion artefact. Patients were all identified from the Health Quality Improvement Partnership National Vascular Registry (NVR), a prospectively maintained database, from January 2008 and December 2014 (9). Inclusion into the study

required the patient to have an abdominal CT with the psoas muscle clearly identifiable from the second lumber vertebrae to the sacrum. Patients were excluded if they had incomplete imaging with missing portions. Ethical approval was granted by the local radiology research authorisation group and Health Research Authority (IRAS project ID, 228484).

Covariate assessment

Data were reviewed from the NVR for baseline age, gender, height and weight. These are all parameters that are routinely collected, however, medical records were also reviewed to ensure all data collected was accurate.

Image analysis

Imaging was performed using a Siemens Somatom Definition AS CT scanner with the patient in the supine position with a breath-hold to minimise motion artefact. Slice thicknesses were between 1mm - 2.5mm. Scans were assessed for inclusion by a single investigator, who did not participate in any images analysis, using the picture archiving and communications system (PACS) viewer IMPAX (AGFA-Gevaert Group, Mortsel, Belgium) and ImageJ (National Institute of Health, Bethesda). Two independent observers (Rater 1 [R1] and Rater 2 [R2]) were trained by an investigator with prior expertise. R1 was a clinician with two years postgraduate clinical experience and R2 was a postgraduate research fellow with 3 years postgraduate clinical experience. The trainer was a surgical fellow with five years postgraduate clinical experience.

TPMA was measured by manually tracing around the area of the left and right psoas muscle at each vertebral level of the transverse processes from L2 to the sacrum (figure 1). TPMV was calculated by multiplying each individual TPMA by the distance between the corresponding

vertebral levels. TAMA was measured using a fully automated technique. In brief, single slice images at the third lumbar vertebrae were downloaded in the digital imaging and communications in medicine (DICOM) format with preservation of actual dimensions to avoid magnification indices and scales. Analysis was subsequently performed using ImageJ (National Institute of Health, Bethesda) by setting the Hounsfield unit (HU) range between -30 to 130 (8). TAMA was calculated by measuring all the abdominal muscles, namely: psoas, erector spinae, quadratus lumborum, transversus abdominis, external and internal oblique's, and rectus abdominis muscles based on the total pixel densities (figure 2). We acknowledge that there are a variety of other software packages and methods that may also be used.

Statistical analysis

Measurements were made in centimetres (cm). TPMA and TAMA are reported as an area (cm^2) and TPMV as a volume (cm^3). Statistical analyses were performed using Minitab 17 (Minitab Inc., Pennsylvania) (10). Continuous variables were checked for normality and reported as a mean and SD or 95% confidence interval (CI). Non-parametric data was reported as a median and interquartile range (IQR). Categorical variable are reported as absolute numbers (n) and percentages (%), and were compared using the chi-square test. Statistical significance was defined as a two-tailed p-value <0.05.

Fifty images were analysed by two trained independent investigators (R1 and R2) to measure the TPMA, TAMA and TPMV. Repeat measurements of all images were made by Rater 1 (for example, R1a and R1b). Intra-observer and inter-observer differences were evaluated using Bland-Altman plots and differences in measurements evaluated using student's t-test. The limits of agreement were calculated as two standard deviations (SD) from the mean difference calculated between observer measurements.

We calculated that we would require at least 85 patients in this study in order to assess for a correlation of greater than 0.7 with 95% significance at 80% power. All images were analysed by R1. Comparisons between the individual methods of assessing core muscle were evaluated using measurements recorded by Rater 1 as single observer measurements are likely to represent clinical practice. The relationship between TPMV and TPMA: at the second lumbar vertebrae (L2), third lumbar vertebrae (L3), fourth lumbar vertebrae (L4), fifth lumbar vertebrae (L5) and sacrum were assessed using Pearson's correlation and linear regression analysis. Similarly, the relationship between TPMA versus TAMA were assessed using Pearson's correlation and linear regression analysis. All regression analyses were adjusted for age and sex.

Results

Patient characteristics

In total, CT scans from 110 consecutive patients were analysed in this study. Scans were performed between October 2008 and July 2014. The median age of patients was 77.5years (IQR 71.3 - 81.0) and there were 96 (87.3%) men. The median height was 174.0cm (IQR 165.5 - 179.0) and the medium weight was 77.0kg (IQR 69.0 - 95.0).

Intra-observer and inter-observer differences

Intra- and inter observer difference are shown in figure 3. No significant differences in measurements were identified between observers (table 1). Single observer variation (R1) was

lowest with TAMA (mean 309.1 cm^2 ± 0.1 [0.03%]), followed by TPMA (mean 8.8 cm^2 ± 0.3 [3.7%]) and then TPMV (mean 337.4 cm^3 ± 13.6 [4.0%]).

Comparative analysis

Measurements of TPMV, TPMA and TAMA were all normally distributed. Mean measurements of the TPMA at each vertebral level, L2 to the sacrum, are highlighted in table 2. As anticipated, men had larger psoas muscle size than women (table 2). The mean TPMV was 334.0 ± 101.6cm^3 and the mean TAMA was 303.7 ± 62.2cm^2. The mean distance between measurements at the: sacrum and L5 was 4.9 ± 1.0cm, L5 to L4 was 4.5 ± 0.9cm, L4 to L3 was 4.3 ± 0.8cm, L3 to L2 was 3.3 ± 0.9cm and L2 to first lumber vertebrae was 3.2 ± 0.9cm.

Significant positive correlations were observed between measurements of TPMV and TPMA at all levels, L2 to sacrum (figure 4). Regression analysis highlighted significant associations between measurements of the TPMA, from L2 to the sacrum, with TPMV (table 3). The greatest association between single slice measurements and volumetric analysis was seen at L3 (unadjusted regression coefficient 20.1, 95% CI 15.4 to 24.9, $p<0.001$, adjusted regression coefficient 16.7, 95% CI 12.1 to 21.4, $p<0.001$).

There was no significant correlation between TPMA and TAMA (figure 5). No association was evident when comparing measurements of TPMA and TAMA (unadjusted regression coefficient 2.9, 95%CI -0.8 to 6.6, $p=0.126$ and adjusted regression coefficient -0.7, 95%CI -4.1 to 2.8, $p=0.710$).

Discussion

In this study, we demonstrate single slice measurements of the TPMA to be representative of the TPMV on CT imaging. Measurements of the TPMA at any vertebral level between L2 to the sacrum were found to be significantly representative of the TPMV. Therefore, it may be plausible to use measurements of TPMA at any of these levels when limited by the images available from routine imaging. This is important as it may not always be possible to measure the TPMA at the L3 vertebrae if the CT sequence has not captured this section. However, it is important to appreciate that the observed regression coefficients and confidence interval were almost identical for TPMA measurements at L3 and L4 therefore utilisation of measurements at either level is acceptable.

Our research adds to the growing body of evidence utilising the measurements of core abdominal muscles from imaging as a surrogate marker for sarcopenia. Shen et al previously demonstrated the association between measurements of the TAMA 5cm above the L4-L5 junction to be associated with volumetric measurements of the abdominal muscle volume on CT imaging in a healthy cohort of patients (3). These finding were confirmed by Mourtzakis et al who demonstrated the relationship between single slice imaging of fat free mass to whole body fat free mass (4). However, it must be noted that these measures were validated on either a normal cohort of people or cancer patients. Despite the correlation between single slice TAMA and abdominal muscle volume, few studies have demonstrated the correlation between single slice measurements of the TPMA and the TPMV. In this study, we have demonstrated a relationship between TPMA and TPMV, and have identified that the measurement of TPMA at L3 (the most widely used level) is most representative of the TPMV. Our group has previously shown that the measurement of TPMA is reproducible and independent of observer bias (8).

Similar to the findings of Rutten et al, we demonstrate no correlation between single slice measurements of TPMA and TAMA (11). Therefore, studies evaluating outcomes in relation to sarcopenia utilising these different measures cannot be reliably compared. We have previously reported that measurements of the TPMA may be easily performed by manually tracing around the psoas muscle at the third lumbar vertebrae without the need for specialist software or clinical experience (8). Therefore, we would recommend the routine measurement of the TPMA for the quantification of sarcopenia as it may be easily utilised in clinical practice.

Similar to previous studies, we demonstrate that women have lower measurements of the psoas muscle in comparison to men. The number of women in our study were too few to allow for assessment of whether these relationships identified by gender were statistically relevant. However it is important to acknowledge that the study was powered to detect the associations between TPMA and TPMV as well as TPMA and TAMA.

However, measurements of TPMA had the lowest variation when compared to TPMV as demonstrated by percentage variation of the standard deviation against the mean intra-observer measurements. This finding is expected as due to the compounding effect of errors accumulating at each level analysed. The utilisation of the TPMA as an assessment tool for sarcopenia instead of TPMV may also facilitate and reduce the numbers needed for patient recruitment when powering future prospective studies. Although TAMA had the least variation, this was primarily due to a completely autonomous method of measurement which may not be routinely applicable out of the research setting.

It is important to acknowledge that our study estimates the TPMV as we did not utilise specialist software as described in previous studies (12). The TPMV was calculated as blocks

based on two-dimensional assessment of the psoas muscle at each vertebral level and then multiplying the area by the distance between vertebral levels. This was intentional as we wanted to replicate the potential real-life application of risk stratification using the psoas muscle as not all clinicians in the National Health Service in the United Kingdom have access to specialist software for this type of image analysis. We acknowledge that this might be a crude measurement given the large interslice distances.

Conclusions

In conclusion, we demonstrate an association between measurements of TPMA and TPMV. Measurements of TPMA may be made at any vertebral level between the sacrum and L2 and be reflective of the TPMV, with the greatest association at L3. We also demonstrate the absence of any association between TAMA and TPMA therefore outcomes reported with either measure cannot be reliably compared and results translated.

FIGURES AND TABLES

Figure 1. Illustration of TPMV calculated from L2 to sacrum. Red line shows manual tracing of TPMA. Example shows TPMA at L2 (4.2cm^2), L3 (10.0cm^2), L4 (16.8cm^2), L5 (22.4cm^2), Sacrum (23.1cm^2). Distances: 2.9cm between L1 and L2, 3.1cm between L2 and L3, 4.4cm between L3 and L4, 5.0cm between L4 and L5, 5.3cm between L5 and sacrum. Therefore, the TPMV calculated is 351.5cm^3.

Figure 2. TAMA measurement using the automated technique. Red highlights tissue matching pixel density with HU between -30 to 130.

Figure 3. Bland-Altman plots showing intra- and inter- observer differences in measurements of TPMA, TAMA and TPMV.

Figure 4. Scatter graph illustrating relationship between TPMV and single slice TPMA measurements at: (a) L2, (b) L3, (c) L4, (d) L5 and (e) sacrum.

Figure 5. Scatter graph demonstrating the relationship between TPMA and TAMA.

Table 1. Observer measurements of TPMA, TAMA and TPMV.

Measurement	R1a	R1b	R2	Intra-observer differences		Inter-observer differences	
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	p-value	Mean (SD)	p-value
TPMV [cm^3]	337.6 (105.3)	337.1 (101.0)	338.8 (106.6)	0.5 (13.6)	0.981	-1.1 (11.8)	0.957
TPMA [cm^2]	8.8 (3.5)	8.9 (3.6)	8.8 (3.4)	-0.03 (0.3)	0.963	0.03 (0.3)	0.924
TAMA [cm^2]	309.1 (66.8)	309.0 (66.7)	309.1 (66.8)	0.1 (0.1)	0.997	-0.003 (0.01)	1.000

Table 2. Measurements of TPMA from L2 to the sacrum by gender.

Spinal level	TPMA			
	Male (N=96)	Female (N=14)	p-value	Overall
L2 [cm^2]	2.6 ± 1.8	1.7 ± 1.4	0.058	2.5 ± 1.8
L3 [cm^2]	9.4 ± 3.1	6.3 ± 2.4	<0.001	9.0 ± 3.2
L4 [cm^2]	16.9 ± 4.2	12.2 ± 3.7	<0.001	16.3 ± 4.4
L5 [cm^2]	23.8 ± 5.2	17.0 ± 4.5	<0.001	22.9 ± 5.6
Sacrum [cm^2]	25.6 ± 5.7	18.5 ± 5.3	<0.001	24.7 ± 6.1

Table 3. Linear regression analysis comparing measurements of TPMA from L2 to sacrum in relation to TPMV.

Spinal level	Unadjusted			Adjusted		
	Regression coefficient	95% CI	p-value	Regression coefficient	95% CI	p-value
L2	16.7	6.2 – 27.2	0.002	12.1	2.6 – 21.5	0.013
L3	20.1	15.4 – 24.9	<0.001	16.7	12.1 – 21.4	<0.001
L4	17.7	14.9 – 20.6	<0.001	15.6	12.5 – 18.7	<0.001
L5	14.1	12.0 – 16.3	<0.001	12.9	10.3 – 15.5	<0.001
Sacrum	11.8	9.5 – 14.0	<0.001	10.3	7.6 – 12.9	<0.001

*Adjusted for age and sex.

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Figure1

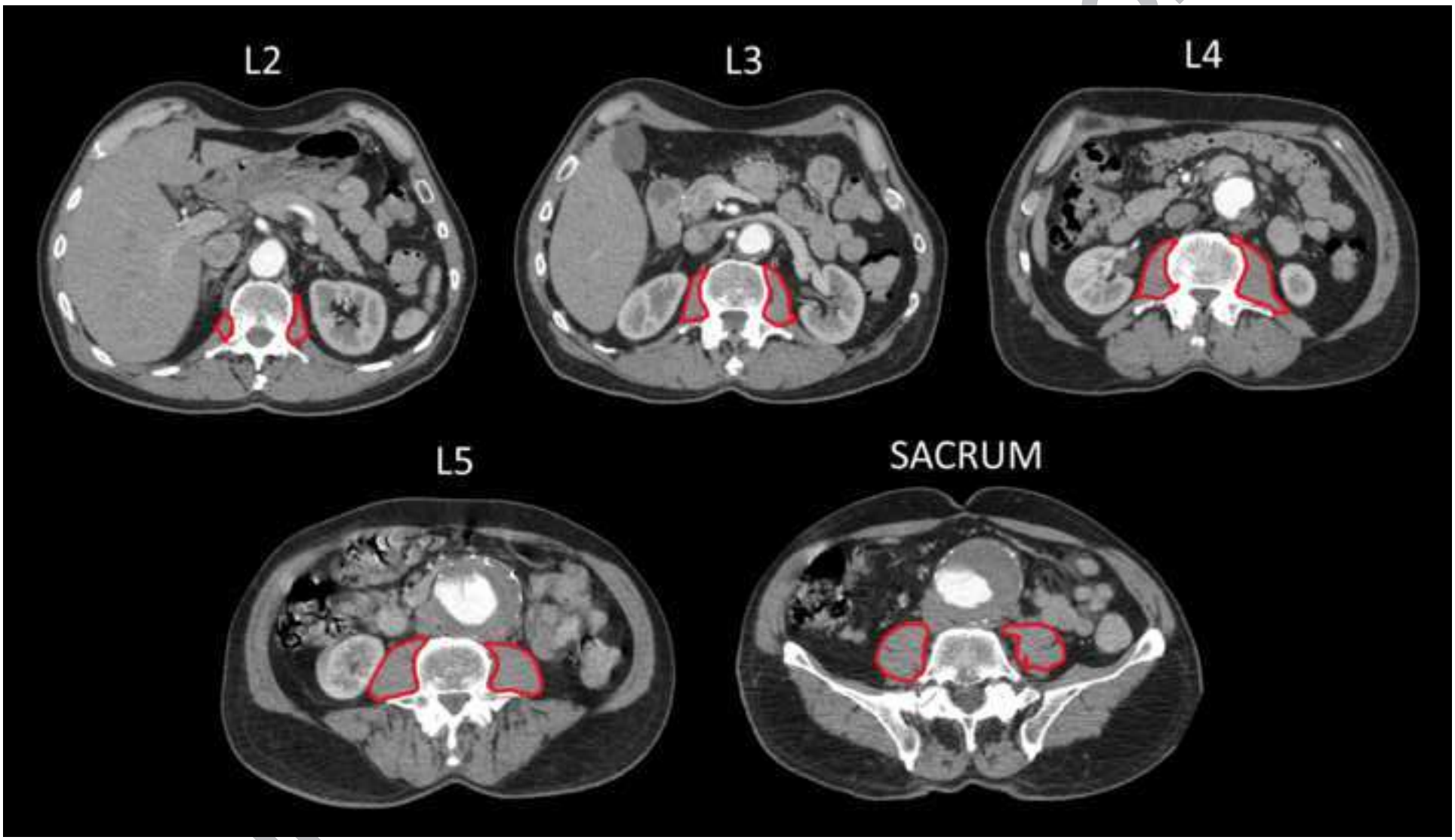

Figure2

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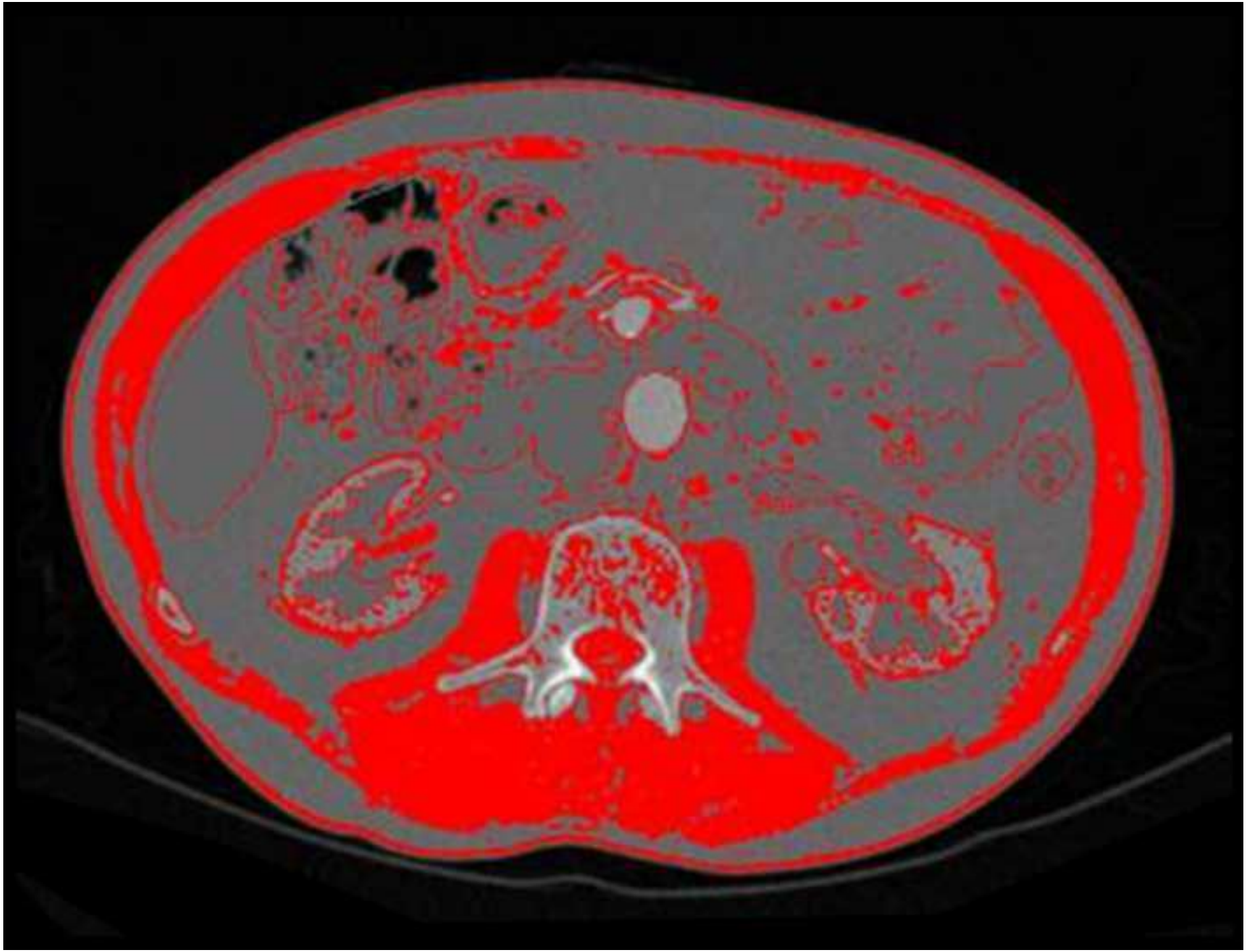

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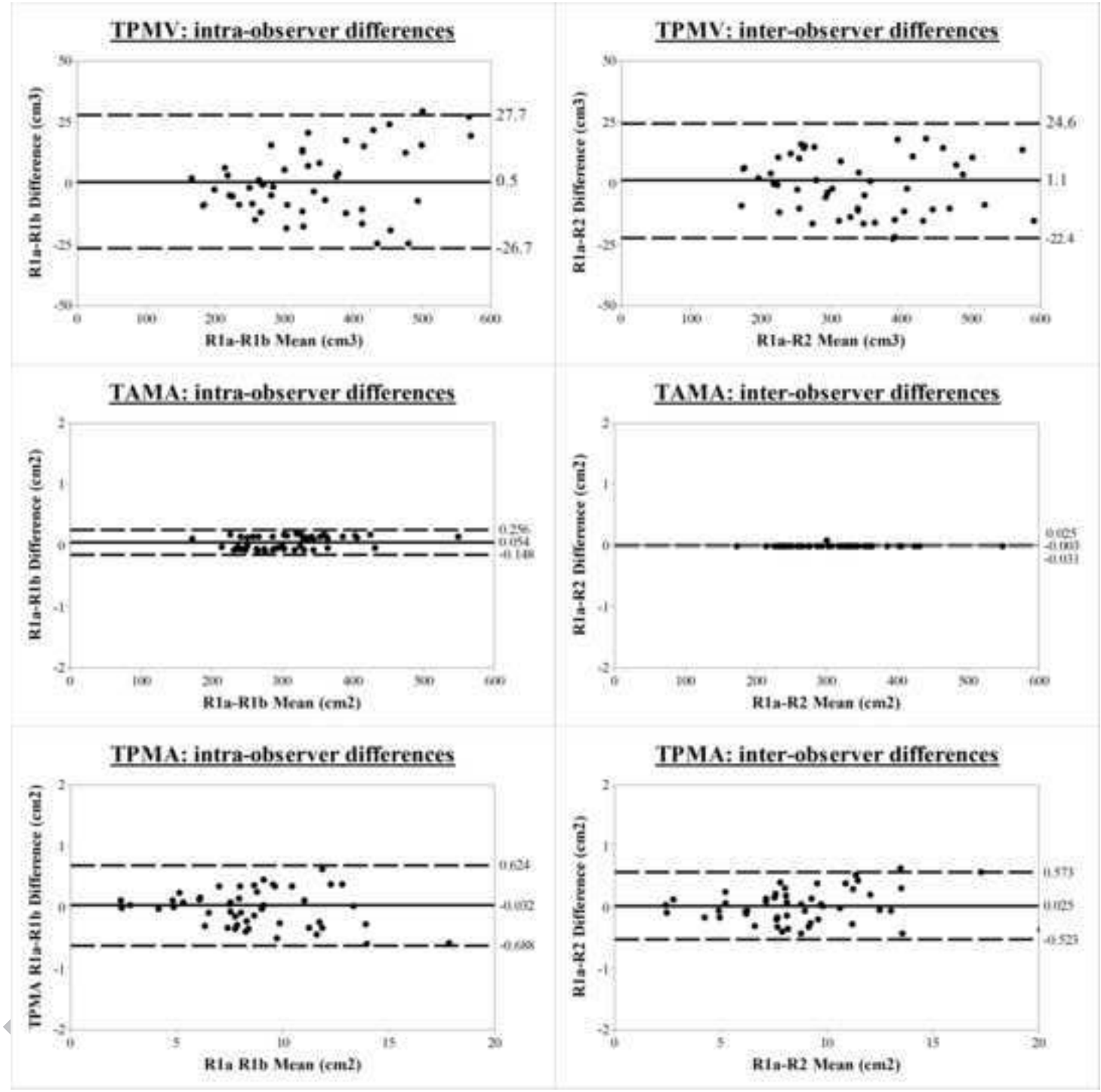

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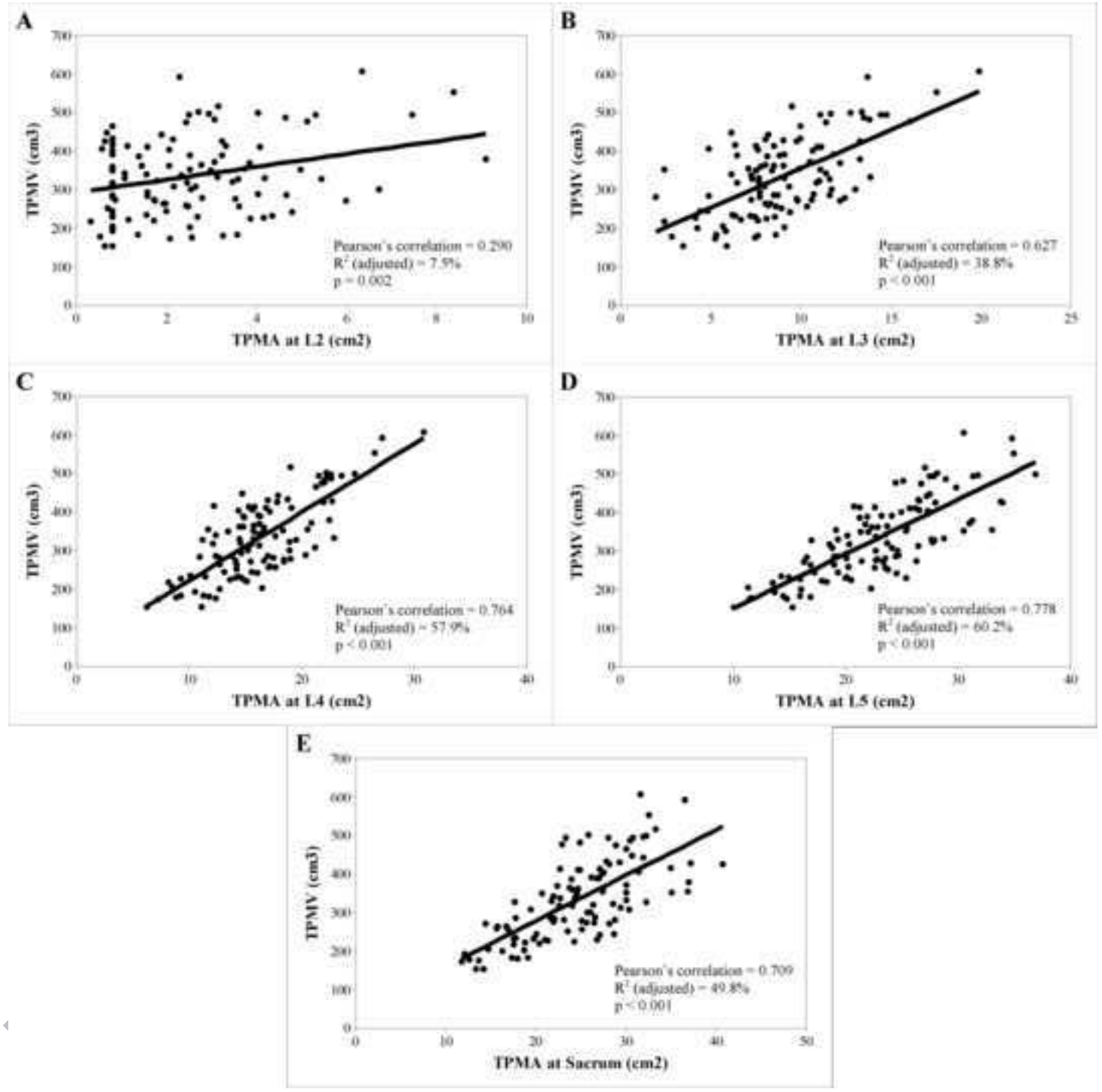

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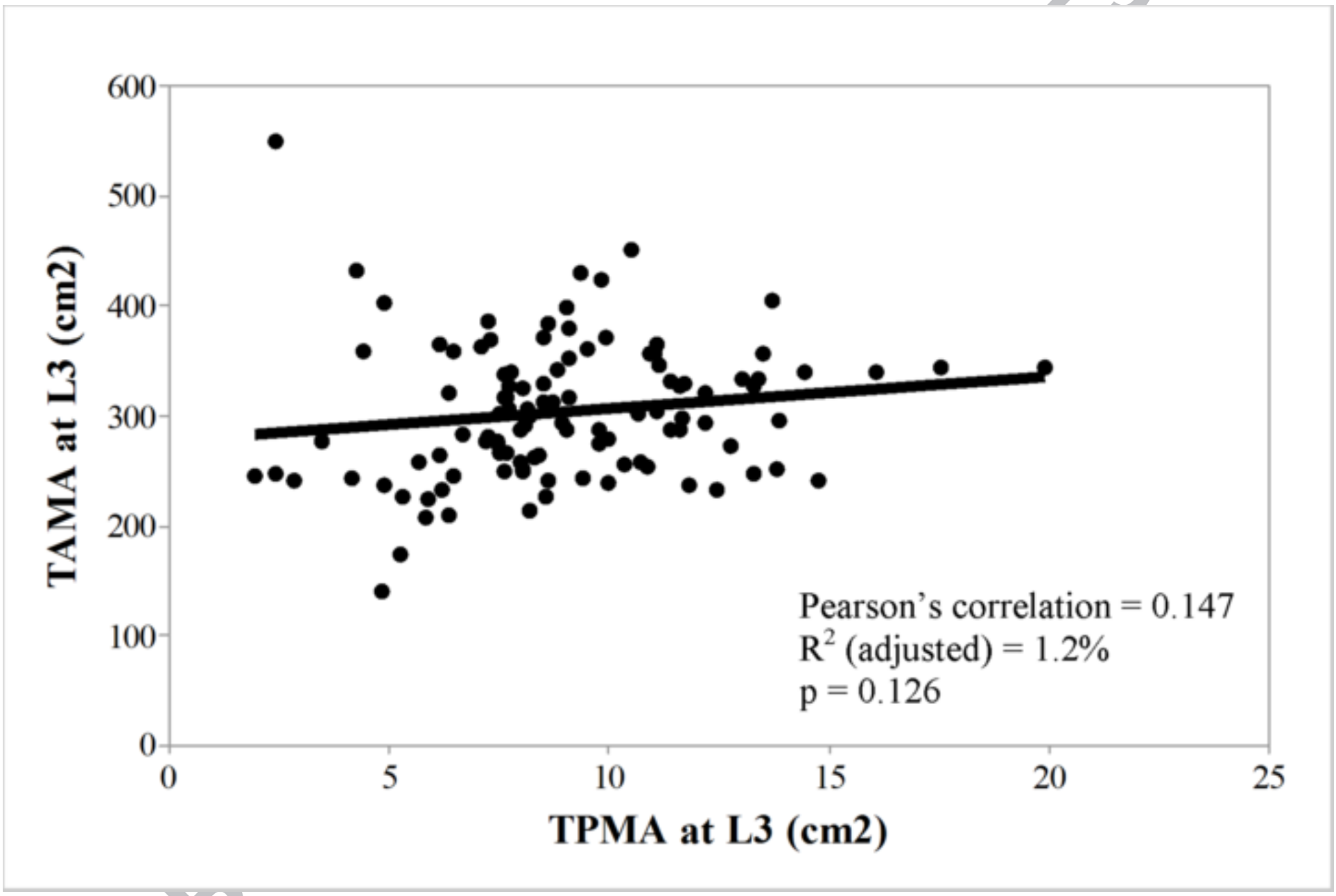

Take home points